

3 - 48 High-LET Radiation Induced Mitophagy and Mitochondrial Apoptosis in Breast Cancer Cells

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To elucidate mitochondrial damage induced by high-LET radiation, human breast cancer MDA-MB-231 and MCF-7 cells were irradiated with carbon ions of 75 keV/ μm at different doses. Mitochondrial $\Delta\Psi_m$ was stained by JC-1 and measured by means of flow cytometry at 1, 4 and 24 h after irradiation, respectively. We found that $\Delta\Psi_m$ had no or a slight change when the radiation dose was as low as about 0.2 or 0.5 Gy at any time point while dissipating at higher doses in MDA-MB-231 cells (Fig. 1). This suggests that the mitochondrial membrane potential had no significant change under low stress conditions. However, high levels of cell stress led to the serious mitochondrial dysfunction. Mitophagy was quantified by the colocalization of lysosomes and mitochondria. As shown in Fig. 2, in cells irradiated at 0.5 Gy, the number of colocalized spots was significantly higher at 12 and 24 h than control group while returning to the control level at 48 h. However, the number of spots was significantly lower than control group after irradiation at high dose. On the contrary, the apoptotic rates of MDA-MB-231 and MCF-7 cells induced by carbon ions were significantly higher at the high dose than those induced at the low dose at 24 and 48 h post-irradiation (Fig. 3).

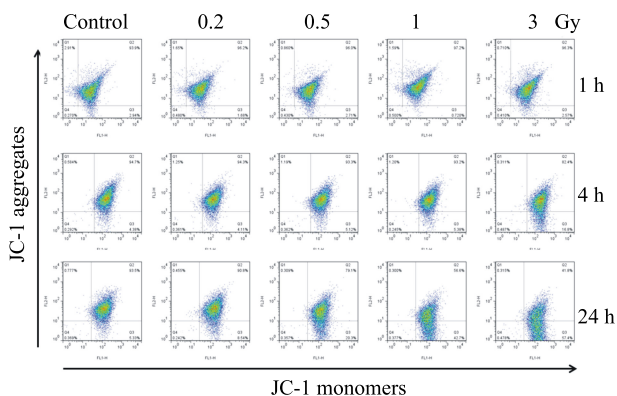


Fig. 1 (color online) JC-1 changes in MDA-MB-231 cells exposed to carbon ions at various doses.

ages, depending on the different stress levels. Under low stress conditions, mitophagy entails the wholesale elimination of damaged mitochondria. Moreover, high levels of cell stress lead to apoptosis via the mitochondrial pathway.

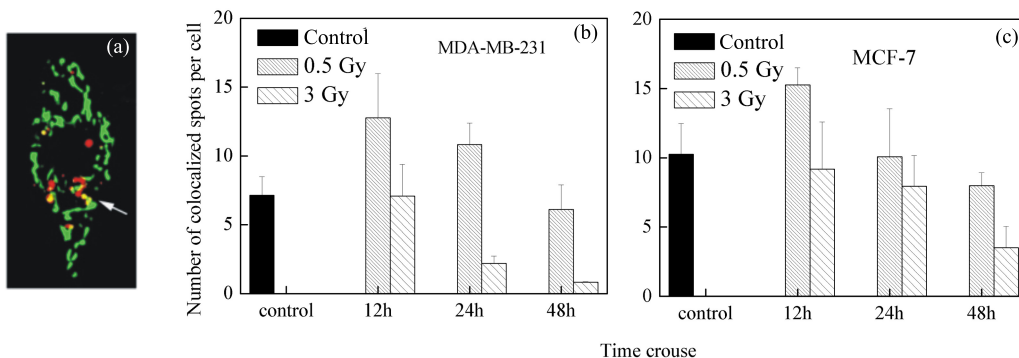


Fig. 2 (color online) Mitophagy induced by high-LET radiation. (a): representative image displaying colocalized spot (yellow) merged with MTG stained mitochondria (green) and LTR stained lysosomes (red), (b) and (c): the number of colocalized spots per cell at 12, 24 and 48 h after irradiation in MDA-MB-231 and MCF-7 cell lines, respectively.

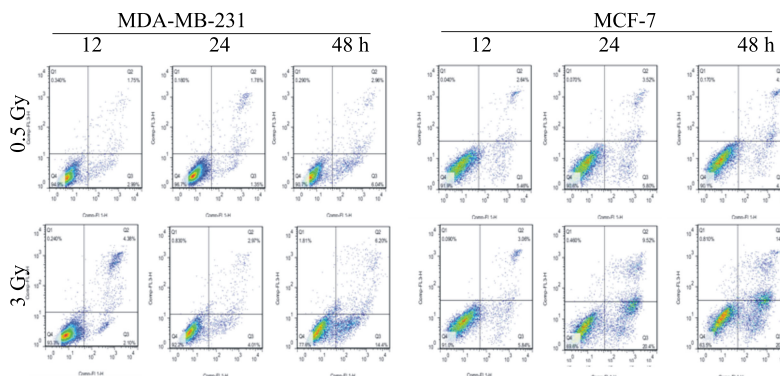


Fig. 3 (color online) Apoptosis induced by high-LET radiation.